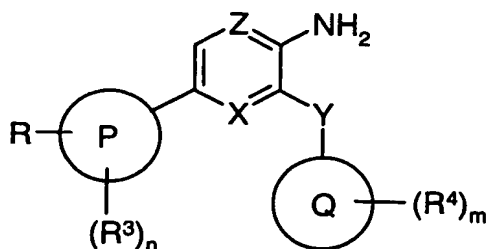


CLAIMS

1. A compound having the formula I



wherein:

Z is N;

10 Y is CONR⁵, NR⁵CO, SO₂NR⁵, NR⁵SO₂, CH₂NR⁵, NR⁵CH₂, NR⁵CONR⁵, C₁₋₆alkylene, CH₂CO, COCH₂, CH=CH, OCH₂ or CH₂O;

X is CH or N;

15 P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O or S and said phenyl ring or heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing one or more atoms selected from C, N, O or S;

20 Q is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more nitrogen atoms and said phenyl ring or heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing one or more atoms selected from C, N, O or S;

25 R is C₁₋₆alkylNR¹⁰R¹¹ or C₁₋₆alkylazetidine which azetidine ring may be optionally substituted by A;

R^3 and R^4 are independently selected from halo, nitro, CHO, C_{0-6} alkylCN, OC_{1-6} alkylCN, C_{0-6} alkylOR⁶, OC_{1-6} alkylOR⁶, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkylNR⁶R⁷, OC_{1-6} alkylNR⁶R⁷, OC_{1-6} alkylOC₁₋₆alkylNR⁶R⁷, NR⁶OR⁷, C_{0-6} alkylCO₂R⁶, OC_{1-6} alkylCO₂R⁶, C_{0-6} alkylCONR⁶R⁷, OC_{1-6} alkylCONR⁶R⁷, OC_{1-6} alkylNR⁶(CO)R⁷, C_{0-6} alkylNR⁶(CO)R⁷, O(CO)NR⁶R⁷, NR⁶(CO)OR⁷, NR⁶(CO)NR⁶R⁷, O(CO)OR⁶, O(CO)R⁶, C_{0-6} alkylCOR⁶, OC_{1-6} alkylCOR⁶, NR⁶(CO)(CO)R⁶, NR⁶(CO)(CO)NR⁶R⁷, SR⁶, C_{0-6} alkyl(SO₂)NR⁶R⁷, OC_{1-6} alkylNR⁶(SO₂)R⁷, OC_{0-6} alkyl(SO₂)NR⁶R⁷, C_{0-6} alkyl(SO)NR⁶R⁷, OC_{1-6} alkyl(SO)NR⁶R⁷, SO₃R⁶, C_{0-6} alkylNR⁶(SO₂)NR⁶R⁷, C_{0-6} alkylNR⁶(SO)R⁷, OC_{1-6} alkylNR⁶(SO)R⁷, OC_{0-6} alkylSO₂R⁶, C_{0-6} alkylSO₂R⁶, C_{0-6} alkylSOR⁶, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl, wherein any C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl may be optionally substituted by one or more A;

m is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^5 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl, C_{1-6} alkylNR⁶R⁷ or C_{1-6} alkylCONR⁶R⁷;

R^6 and R^7 are independently selected from hydrogen, C_{1-6} alkyl, (CO)OR⁸, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl and C_{1-6} alkylNR⁸R⁹;

R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkylC₃₋₆cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

- 5 R^{10} is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl or C_{1-6} alkyl NR^8R^9 ;

R^{11} is C_{0-6} alkyl C_{3-6} cycloalkyl;

- 10 A is halo, nitro, CHO, CN, OR^6 , C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkyl NR^6R^7 , OC_{1-6} alkyl NR^6R^7 , CO_2R^8 , $CONR^6R^7$, $NR^6(CO)R^6$, $O(CO)R^6$, COR^6 , SR^6 , $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6 , SO_2R^6 or SOR^6 ;
- 15 as a free base or a pharmaceutically acceptable salt, solvate or solvate of salt thereof.

2. A compound according to claim 1, wherein Z is N; Y is $CONR^5$; X is N; P is phenyl; Q is a 6 membered aromatic heterocyclic ring containing one nitrogen atom; R is C_{1-6} alkyl $NR^{10}R^{11}$; m is 0; n is 0; R^5 is hydrogen; R^{10} is hydrogen or C_{0-6} alkyl C_{3-6} cycloalkyl; C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl or C_{1-6} alkyl NR^8R^9 ; and R^{11} is C_{0-6} alkyl C_{3-6} cycloalkyl.
- 20

3. A compound according to claim 2, wherein C_{1-6} alkyl in C_{1-6} alkyl $NR^{10}R^{11}$ represents propyl; R^{10} and R^{11} represents cyclobutyl; and Q represents pyridin.

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4. A compound which is:

3-Amino-6-{4-[3-(dicyclobutylamino)propyl]phenyl}-N-pyridin-3-ylpyrazine-2-carboxamide hydrochloride;

as a free base or an alternative pharmaceutically acceptable salt, solvate or solvate of salt thereof

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5. A compound which is:

3-Amino-6-bromo-*N*-pyridin-3-ylpyrazine-2-carboxamide;

as a free base, a salt, solvate or solvate of a salt thereof.

5

6. A compound which is:

N-[3-(4-Bromophenyl)propyl]-*N,N*-dicyclobutylamine;

as a free base, a salt, solvate or solvate of a salt thereof.

10

7. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 4 in association with pharmaceutically acceptable carriers or diluents.

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8. The pharmaceutical formulation according to claim 7 for use in the prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

9. A compound as defined in any one of claims 1 to 4 for use in therapy.

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10. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

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11. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica.

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12. Use of a compound according to claim 11, wherein the disease is Alzheimer's Disease.

13. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism,

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progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication.

- 5 14. Use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament for prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairment No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular
- 10 dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia and Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.
- 15 15. A method of prevention and/or treatment of conditions associated with glycogen synthase kinase-3, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.

16. A method of prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle
- 20 pathologies and dementia pugilistica, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.

- 25 17. The method according to claim 16, wherein the disease is Alzheimer's Disease.

18. A method of prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders,
- 30 depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication, comprising administering to a mammal, including man in need of such prevention and/or

treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 4.

19. A method of prevention and/or treatment of predemented states, Mild Cognitive
5 Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline,
Cognitive Impairment No Dementia, mild cognitive decline, mild neurocognitive decline,
Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular
dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia
and Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders,
10 comprising administering to a mammal, including man in need of such prevention and/or
treatment, a therapeutically effective amount of a compound of formula I as defined in any
one of claims 1 to 4.

20. The use of the intermediates according to claim 5 or 6 for the preparation of a
15 compound of formula I as defined in any one of claims 1 to 4.